REMARKS

Applicants have canceled claims 2-4, and amended claims 1, 5 and 13 to more particularly point out and distinctly claim the subject matter of the present invention, without prejudice. Applicants expressly reserve their right to pursue the canceled subject matter in one or more continuing applications that claim priority under 35 USC §120 from this application.

Objections to the Specification

The Examiner objects, as set forth at page 2 of the pending Office Action, to certain informalities in the amendment to the specification filed on 3/4/04. These informalities have been corrected by the amendments *supra*.

Rejections Under 35 USC §112, 2d paragraph

Claims 1-5 and 13 are rejected under 35 USC §112, 2d paragraph as indefinite "for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (Office Action at 3). Specifically, the Examiner objects to the phrases "capable of participating in the human PTCH/SHH pathway" in claims 1-4, and "essentially comprised of SEQ ID NO:1" in claim 1. This rejection has been obviated by the deletion of these phrases from claim 1 and the cancellation of claims 2-4.

Rejections Under 35 USC §§ 101 and 112, 1st paragraph

Claims 1-5 and 13 are rejected under 35 USC §101 as lacking "either a specific and substantial asserted utility or a well established utility." Specifically, the Examiner states that "[t]he specification as filed does not disclose or provide any evidence that points to an activity for the protein and furthermore there is no art of record that discloses or suggests any activity for the claimed protein" (Office Action at 5).

Applicants respectfully disagree. The Specification as filed does in fact disclose, and provide evidence of, an activity for the protein. Much of this evidence is even set forth by the Examiner in the Office Action itself in the paragraph bridging pages 4-5, including a comparison of the structure and function of human PTCH2 to human PTCH1 and mouse PTCH2. In particular, the Specification states that in basal cell carcinomas (BCCs) having frequent mutations in the PTCH1 gene, the expression of PTCH2 mRNA is upregulated (see Specification, page 23, lines 10-11). The diagnostic value of PTCH2 in view of this teaching would be clear to one of skill in the art.

In addition, the Specification explicitly identifies other utilities for the presently claimed invention. For example, it is disclosed that the PTCH2 gene has been localized to a chromosomal region often lost in tumor types such as neuroblastoma, melanoma, breast cancer, colon cancer etc. PTCH2 is thus a candidate for a tumor suppressor gene in this region, "and the present invention also encompass[es] diagnostic methods based on this new disclosure" (page 13, lines 17-23). The Specification further states that this region is also one to which three cancer disposition syndromes have been mapped. As a result, PTCH2 is also a candidate for the gene behind these hereditary syndromes, "and the present molecules are therefore advantageously used in the context of these conditions, *e.g.* in therapy and/or diagnosis, such as in assays (page 13, lines 24-29). Such therapeutic and diagnostic uses are specific, substantial and credible utilities.

Moreover, even if such disclosure of utility was not sufficient on its own to meet the requirements of 35 USC §101, there is art of record that discloses activity of, and uses for, for the claimed protein. For example, US Patent No. 6,348,575 to de Sauvage et al. (hereinafter "Sauvage", cited by the Examiner in the Office Action in connection with a prior art rejection and discussed in that respect *infra*) sets forth multiple uses for patched-2:

> Patched-2 polypeptides can be used in assays to identify the other proteins or molecules involved in complexing with patched-2 which ultimately results in the modulation of hedgehog signaling. Alternatively, these molecules can modulate the binding of patched-2 to Dhh.... By such methods, inhibitors of the binding interaction can be identified. Proteins involved in such binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.... Screening assays can be designed to find lead compounds that mimic the biological activity of a native patched-2 or to find those that act as a substrate for patched-2. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Such small molecule inhibitors could block the enzymatic action of patched-2, and thereby inhibit hedgehog signaling.

Sauvage, col. 19, l. 66-col. 20, l. 17.

Sauvage also describes the use of patched-2 or a fusion protein thereof as the immunizing agent to elicit polyclonal or monoclonal anti-patched-2 antibodies (*Id.* at col. 21, l. 46-col. 26., l. 19). Such antibodies are said to "have utilities corresponding to those articulated previously for patched-2" including, *inter alia,* use in the treatment of BCC (*Id.* at col. 26, 9-14).

In a further example of the well-established utility of patched-2, US Patent No. 6,309,879 to Bumcrot notes that patched-2 proteins "facilitate[ ] the development of assays which can be used to screen for drugs which are either agonists or antagonists of the normal cellular function of the subject ptc-2 proteins, or of their role in the pathogenesis of cellular maintenance, differentiation and/or proliferation and disorders related thereto" (Bumcrot, col. 28, ll. 62-67).

The Examiner refers, at page 7 of the Office Action, to Example 4 of the Utility Guidelines for support of the instant utility rejection. But Example 4 clearly is not analogous to the present invention. In Example 4, an amino acid sequence is claimed without *any* disclosed or well-established utility, or description of its chemical, physical, or biological properties other than the sequence. In response to rejections under sections 101 and 112, first paragraph, the Applicant in Example 4 refers only to a vague general utility as "a source of amino acids used for manufacturing supplements for vitamins or food, as protein supplements for animal food, or as an animal poison if the protein is toxic" that would be equally applicable to any amino acid sequence. Applicants have gone far beyond what is set forth in Example 4, describing utilities specific to PTCH2 in the present application, and citing other well-established utilities *supra*. Extensive information on the chemical, physical and biological properties of the PTCH2 protein has also been provided, by way of comparison to similar known proteins. Nothing in Example 4 of the Utility Guidelines supports the rejection of the present invention on §101 or §112, first paragraph grounds.

The Office Action alleges a lack of guidance in the specification and criticizes the working examples in support of the rejection under 35 USC §112, first paragraph (Office Action at 13-24). The bases for these allegations is essentially the same as the rationale for the 35 USC §101 rejection, and is traversed by Applicants for the same reasons set forth above in connection with the 35 USC §101 rejection.

To the extent that the §112, first paragraph rejection is based on an alleged lack of teaching concerning "a protein comprising at least 1000, 1040, or 1100 amino acids of SEQ ID NO:1," the rejection is rendered moot by the cancellation of claims 2-4.

In summary, when reasonably interpreted in view of the knowledge in the art, and considering the high level of skill in the art, the present invention is useful and no undue experimentation is required to make or use it. Accordingly, reconsideration and

withdrawal of both the §101 and §112, first paragraph rejections are respectfully requested.

Rejections Under 35 USC §102

Claims 1 and 5 stand rejected over Sauvage. At page 16 of the pending Office Action the Examiner, alleging that the "essentially comprised of" language in original claim 1 is indefinite, interprets it to mean "comprising sequences that are essentially similar to SEQ ID NO:1." As a result of that interpretation, the Examiner asserts that "the patched-2 polypeptide of SEQ ID NO.2 of de Sauvage reads on the instant inventions."

Without conceding the correctness of the Examiner's argument, it is believed that the amendment of claim 1 to eliminate the "essentially comprised of" language renders this rejection moot. The presently claimed sequence is neither taught nor suggested by Sauvage. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

Applicants respectfully submit that the application as amended is in condition for allowance, and early, favorable action is respectfully requested. In the event that there are any questions relating to this Amendment or to the application in general, the Examiner is requested to telephone the undersigned concerning such questions so that the prosecution of this application can be expedited.

Respectfully submitted,

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